REMARKS

Reconsideration of this application and reexamination of the pending claims in view of the amendments and remarks herein are respectfully requested. The listing of claims provided herein cancels claims 24, 25, 74, 75, 79, 80, 92, 93, and 96-101; amends claims 23, 29, 32, 34, 78, 81, 84, 89, 92, 102, and 103; and adds new claims 104 and 105. The claim amendments are fully supported by the application as filed and do not introduce new matter.

Claims 23, 26-34, 72, 73, 76-78, 81-91, 94, 95, and 102-105 are pending. Of those, claims 31, 72, 73, 76, 77, 86, 90, 91, 94, 95, 102, and 103 are withdrawn from consideration. Applicants submit that new claims 104 and 105 are also drawn to a non-elected invention. Applicants request rejoinder of the withdrawn claims, and new claims 104 and 105, once the independent claims are found allowable.

Claims 23-30, 32-34, 78-85, 87-89, and 96-100 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, which Applicants regard as the invention. Office Action at Item 3. The basis for this rejection is the Examiner's assertion that "DC-SIGN and DC-SIGN receptor are synonymous terms." According to the Examiner, "[t]he acronym, 'DC-SIGN' does not include the term 'receptor'," so it is allegedly "unclear how a ligand (DC-SIGN) and its receptor (DC-SIGN receptor) can be one and the same."

Paragraph 055 of the specification states that, "[i]n the case of humans, 'DC-SIGN receptor' refers generically to DC-SIGN (described in Curtis et al., 2001), and/or DC-SIGNR (described in Pohlmann et al., 2001)." Applicants previously amended their claims to recite "DC-Specific ICAM-Grabbing Nonintegrin" immediately before the first

use of the acronym "DC-SIGN," at the request of the Examiner. To ensure that the claims are even clearer, Applicants have now amended the claims to recite "human" and "one or more DC-SIGN receptor selected from DC-SIGN and DC-SIGNR." At the first use of each of those acronyms in the claims, Applicants wrote out the full name of each molecule, "DC-Specific ICAM-Grabbing Nonintegrin," and "DC-Specific ICAM-Grabbing Nonintegrin Related," respectively. Applicants submit that the claims particularly point out and distinctly claim the subject matter, which they regard as the invention, and submit that this rejection may be withdrawn. Applicants reserve the right to prosecute claims directed to additional subject matter which they regard as their invention, in continuation or divisional applications.

Claims 23-30, 32-34, 78-85, 87-89, and 96-100 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Office Action at Item 4. According to the Examiner, "the method claims are non-enabled for their asserted ability to treat a *Flaviviridae* virus infection *in vivo*." Regarding the Examiner's contention that the claims are not enabled as to all *Flaviviridae* virus infections, Applicants submit that amendment of the claims to recite specifically Dengue virus infections renders that basis of rejection moot. As Applicants will show, the claims are enabled for treatment of Dengue virus infections. In making his amendment Applicants do not concede that claims to treatment of infections by other *Flaviviridae* viruses are not enabled. Applicants are merely making this amendment to expedite prosecution.

The standard for determining whether a specification meets the enablement requirement is whether the experimentation needed to practice the invention is undue or

unreasonable. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988); MPEP 2164.01. "[T]hat experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. " MPEP 2164.01 (internal citations omitted).

The Examiner seems concerned that the amount of experimentation required to practice the claimed invention may be undue. Specifically, the Examiner points to an article by Navarro-Sanchez et al., which reports the inventors' work and is not prior art to this application. The Examiner first acknowledges that the article "discloses that DC-SIGN is essential for the productive infection of human dendritic cells by mosquito-cell-derived dengue viruses." The Examiner then observes that the article "discloses that the relevance of this discovery remains to be tested *in vivo.*" The Examiner appears to feel that the disclosure regarding results obtained *in vitro* provided by the specification will not be sufficient to allow the skilled artisan to practice the claimed invention, *in vivo*. However, Applicants submit that the statement in Navarro-Sanchez et al. merely reflects the ordinary prudence of scientists to not overstate what they have actually proved. However, Applicants need not prove beyond all doubt that their invention is commercially viable. Rather, Applicants specification must enable the skilled artisan to practice the invention as claimed without undue experimentation. *See* M.P.E.P. 2164 ("[T]o comply with 35 U.S.C. 112, first paragraph, it is not necessary to 'enable one of ordinary skill in the art to make and use a perfected, commercially viable embodiment absent a claim limitation to that effect.' Detailed procedures for making and using the

invention may not be necessary if the description of the invention itself is sufficient to permit those skilled in the art to make and use the invention." (citations omitted)).

Regarding alleged unpredictability faced by the skilled artisan in practicing the invention, the Examiner stated that, "[t]he level of predictability in the art is low because the mechanism described in this invention is novel, and thus *in vivo* experimentation is required to determine whether *in vitro* results reflect *in vivo* performance." The Examiner further stated that,

> [t]he specification does not provide guidance for inhibiting virus entry *in vivo*. If one of skill in the art were to treat a flavivirus infection, given the claimed methods and specification, one would not know what dosage of antibody, for example, should be used for binding DC-SIGN. Given the abundance of dendritic cells in an individual, one would have to consider what dosage of antibody would be appropriate for binding a significant number of dendritic cells such that the virus (already present in the body) would be inhibited. Applicant has not taught what effective amount of antibodies would result in a therapeutic benefit for the patient (an improvement in a symptom). Given the fast-acting viral pathology of Dengue virus, one would need to know the effective amount and frequency that would inhibit the binding of virus to dendritic cells.

In response to the Examiner's characterization of uncertainty, Applicants note that making just such determinations is routine in the art. What is not routine, and what Applicants discovered, is the molecular mechanism of Dengue viral entry. Armed with that information and the teachings of the specification, the skilled artisan can practice the invention as claimed. Applicants fully agree that in the ordinary course of doing so the skilled artisan will apply well established techniques to determine what amount of a molecule that specifically binds to the DC-SIGN receptor is sufficient to inhibit the binding of the Dengue virus effector molecule to the DC-SIGN receptor to thereby treat

the Dengue virus infection. Doing so will not require undue experimentation. The Examiner appears to suggest that finding such a dosage would be undue, but does not provide any rationale of why that would be so. Applicants submit that the skilled artisan could make just such a determination, first conducting further *in vitro* studies, then conducting studies in rodents, and ultimately conducting further studies in humans. That is the ordinary course of taking a discovery and commercializing it and is not undue experimentation.

The Examiner also cited articles that state that vaccines against Dengue virus were not known and that little was known about flavivirus entry into cells. In relying on those disclosures the Examiner ignores the fact that the Inventors' discovery changed and improved on the state of the art, and provided an explanation for flavivirus entry into cells. As part of the *quid pro quo* of obtaining the rights to be conferred by their patent, the inventors will share this knowledge they have gained with the public and thus enable the skilled artisan to apply that knowledge and practice their invention based on their teachings, and knowledge in the art as described above. On the basis of their discovery, Applicants invented methods of treating Dengue virus infection and preventing entry of Dengue virus into cells. That no one else made their invention first reflects that their invention is new but does not show that their invention is not enabled.

Applicants also note that claim 78 recites "inhibiting entry of a Dengue virus into a cell of a human," and "wherein entry of the Dengue virus into the cell of the human is mediated at least in part by binding of a Dengue virus effector molecule on the Dengue virus to the DC-SIGN receptor on the cell of the human." That method does not require a specific therapeutic outcome, but rather a mechanistic outcome—viral entry is

inhibited. The experiments reported in the specification show that this result is obtained using the methods disclosed. Thus, in additional to many variations enabled by the specification, the skilled artisan need only practice what is expressly disclosed in order to practice this invention. Therefore, claim 78, and claims 81-95, 98-100, and 102, which depend from claim 78, are all enabled for this additional reason.

For the foregoing reasons, Applicants submit that the amended claims are enabled and request that the rejection for alleged lack of enablement be withdrawn.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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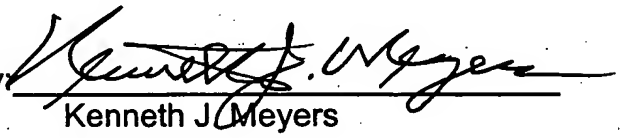
By: 

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